REMARKS

This amendment is submitted in an earnest effort to bring this case to issue without delay.

Applicants have canceled claims 1 through 8, 14 through 20, and 26 through 28 and added new claims 29 through 39. Antecedent basis for claims 28 through 39 may be found in the specification on page 4, line 22 through page 21, line 12, and in Examples 1 through 5 on pages 23 through 31. Page 6, lines 11 to 21 provides special antecedent basis for claim 38. Thus claims 29 through 39 are now in the application and are presented for examination.

Applicants have drafted new claims 29 through 39 in order to respond to the Examiner's rejection of the claims last presented under 235 USC 112, first paragraph. All claims now presented are believed to comply with the written description requirement of 35 USC 112, first paragraph, in that Applicants were clearly in possession of the invention as now claimed, when they filed this application. In claims 29 through 34 now presented Applicants have limited the nucleotide sequence to SEQ ID NO: 1 which encodes L-serine dehydratase, but having nucleotides from position 506 to position 918, completely or partially deleted or mutated, so that the L-serine dehydratase is expressed to a lesser extent than expressed by the naturally occurring SEQ ID NO: 1 or not expressed at all. The gene structures and vectors containing the nucleotide

sequence SEQ ID NO: 1 have also been so limited. The specification on page 5, line 14 to page 8, line 22, page 10, line 21 to page 13, line 20, page 15, line 16 to page 16, line 16, the drawings that are Figures 1 and 3 and the specific description of the drawings on pages 21 and 22, as well as the specific examples 1 through 5. No longer are applicants attempting to claim a polynucleotide where the entire SEQ ID NO: 1 has been deleted and no longer are Applicants attempting to claim a single polynucleotide that includes both serine biosynthesis genes and SEQ ID NO: 1.

In addition the recombinant microorganisms now presented in claims 35 through 38 have been limited to Corynebacteria, and claims 35 through 37 sharply limit the identity of both the SEQ ID NO: 1, that is the L-serine dehydratase gene, as well as the serine biosynthesis genes SerA, SerB, and SerC, all of which are clearly defined as originating from Corynebacteria. Furthermore claims 35 and 38 specifically define the flanking sequences SEQ ID NO: 3 and SEQ ID NO: 6 necessary for the homologous recombination for introducing the novel form of the polynucleotide that is SEQ ID NO: 1 into the Corynebacterium. See page 23, line 16 through page 24, line 2 for the antecedent basis. In the case of the recombinant microorganism that is covered in claim 38, in this particular microorganism the polynucleotide sequence that is SEQ ID NO: 1 has been deleted in its entirety from the recombinant Corynebacterium solely through homologous recombination replacing SEQ ID NO: 1 with the flanking sequences SEQ ID NO: 3 and SEQ ID NO: 6. Since

Applicants are claiming in claim 38 a recombinant microorganism, and not merely a novel form of SEQ ID NO: 1, the entire SEQ ID NO: 1 can be deleted from the microorganism and what remains is still a meaningful invention.

Claim 39 covers the primers or flanking sequences, namely, SEQ ID NOS: 3,4,5 and 6. Again see page 23, line 16 through page 24, line 2 for antecedent basis.

Similarly all claims now presented are believed to comply with the enablement requirement of 35 USC 112, first paragraph. Applicants have limited the definition of the new polynucleotides where SEQ ID NO: 1 but having nucleotides from position 506 to position 918, completely or partially deleted or mutated, so that the L-serine dehydratase is expressed to a lesser extent than expressed by the naturally occurring SEQ ID NO: 1 or not expressed at all. No longer are alleles covered and no longer are Applicants attempting to cover a polynucleotide per se where the entire Seq ID NO: 1 has been deleted. Similarly gene constructs and vectors containing the novel forms of SEQ ID NO: 1 are also in compliance with the enablement requirement. The recombinant microorganisms of claims 35 through 37 are also in compliance with the enablement requirement since the microorganisms are limited to Corynebacteria, the endogenous serine biosynthesis genes are limited to the SerA-fbr, SerB and SerC Corynebacteria serine biosynthesis genes and the new polynucleotides have been limited as defined above. Claim 37 has even been limited to the microorganism is Corynebacterium

Glutamicum of the strain 13032ΔpanBCΔsdaApSerA^{fbr}CB. See Example 1, especially on page 25, line 21 to page 26, line 19 for antecedent basis. Thus the scope of the claims to both the new polynucleotides and to the Corynebacteria into which the new polynucleotides have been homologously recombined now presented bears a reasonable correlation to the scope of the exemplified polynucleotides and recombinant microorganisms in the specification.

In the case of the recombinant Corynebacterium that is covered in claim 38, in this particular microorganism the polynucleotide sequence that is SEQ ID NO: 1 has been deleted in its entirety from the recombinant Corynebacterium solely through homologous recombination replacing SEQ ID NO: 1 with the flanking sequences SEQ ID NO: 3 and SEQ ID NO: 6, thereby deleting SEQ ID NO: 1 in its entirety from the particular Corynebacterium.

The Examiner has rejected claims 14-15 and 17 - 19 as anticipated under 35 USC 102 in view of KUBOTA et al. Applicants have canceled all claims last presented and have submitted new claims 29 through 39. Applicants do not believe that any claim now presented is either anticipated under 35 USC 102 or obvious under 35 USC 103 in view of KUBOTA et al. KUBOTA et al defines L-serine dehydratase activity at the biochemical level (i.e., measuring serine levels in Corynebacterium extracts) and isolates a mutant strain lacking this activity. However, this reference does not map the location of the mutation in the Corynebacteria genome, and does not isolate the Corynebacteria gene(s) encoding L-serine

dehydratase activity. Therefore, it is entirely possible that the strain isolated in this reference carries a mutation in a gene other than sdaA, which is responsible for the observed phenotype of defective dehydratase activity. For instance the mutation that KUBOTA et al induces in the Corynebacterial genome might not even be in the gene encoding L-serine dehydratase, but might be located in the promoter or in some other regulatory gene. There is no way to tell from the KUBOTA reference any specifics at all about the induced mutations.

Thus it is neither disclosed nor suggested in KUBOTA et al to obtain any of the polynucleotides of the structures covered in claims 29 and 30, any of the gene constructs of claims 31 and 32 containing the polynucleotides, any of the vectors of claims 33 and 34 containing the polynucleotides, any of the recombinant microorganisms of claims 37 through 37 containing the polynucleotides, or even the recombinant microorganism of claim 38 wherein the polynucleotide of SEQ ID NO: 1 has been deleted in its entirety. Nor are the primers covered in claim 39 anticipated or rendered obvious by KUBOTA et al.

To establish that the mutation is really in the sdaA, KUBOTA et al would have had to have performed a complementation test which would have to be performed using the mutant strain. For example, a mutation in a transcription factor that controls the expression of sdaA might show a similar phenotype to the one observed by this group, and could fully account for the loss of

dehydratase activity as defined biochemically. However, KUBOTA et al carried out no such test and so there is nothing that is either disclosed or suggested in the reference that would indicate that KUBOTA et al ever obtained an identical structure or a similar structure to any of the polynucleotides that Applicants have obtained or to the gene constructs, vectors, or recombinant forms of Corynebacteria containing those polynucleotides. There is also no disclosure or suggestion in KUBOTA et al to delete the entire sda gene of SEQ ID NO: 1 from the Corynebacteria genome through homologous recombination to obtain the recombinant Corynebacterium of claim 38 and no suggestion in the reference to obtain the primers of claim 39. Thus the reference provides no basis for a rejection of any claim now presented under either 35 USC 102 or 35 USC 103.

The Examiner has also rejected claims 1 through 8, 14 through 20, and 26 through 28 as obvious under 35 USC 103 citing KUBOTA et al in combination with NAKAGAWA et al US 2002/0197605. Applicants have canceled all claims last presented and are submitting new claims 29 through 39 which are believed to be patentbably distinguishable over the cited combination of references. Applicants believe that it is rather surprising that a deletion the nucleotides in positions 506 to 918 of SEQ ID NO: 1 completely switched off the entire L-serine dehydratase. Applicants regard the complete deactivation of the L-serine dehydratase as unexpected from the prior art.

Applicants have already discussed the KUBOTA et al reference hereinabove and those same arguments to distinguish the presently claimed KUBOTA et al reference per se apply as well to the combination of KUBOTA et al and NAKAGAWA et al.

The NAKAGAWA reference from 2002 only shows that the Corynebacterium genome contains a gene that displays sequence homology to serine dehydratases isolated from other species. There is no experimental evidence that either complete deletion of sdaA or loss-of-function mutations in sdaA would lead to decreased serine dehydratase activity, and therefore increased serine production, by Corynebacterium.

For these reasons, the experimental evidence presented by the Applicants constitutes a novel, useful, and unobvious finding. They are the first to show that loss-of-function mutations in Corynebacterium sdaA and even complete elimination of the gene lead to decreased serine dehydratase activity, and therefore increased serine production, by Corynebacterium.

There are many references in the literature that disclose polynucleotides that express enzymes other than L-serine dehydratase which demonstrate that large deletions from an open-reading frame of the gene do not completely switch off enzymatic activity. Thus it is described that deletion of 220 nucleotides in the human insulin receptor kinase still result in expression of a protein with enzymatic activity. See J. Biol. Chem., 1993, Oct. 25; 268(30):22444-9, and it is also described that instead deleting

129 nucleotides of the polynucleotide expressing lactose synthatase, the enzymatic activity still remains intact. See Protein Eng. 1993, Sept. 6, ; (7): 779 to 785. Therefore the fact that Applicants have deleted from the L-serine dehydratase gene having SEQ ID NO: 1 some or all of the nucleotides 506 to 918, and have obtained as a result a mutated SEQ ID NO: 1 with no L-serine dehydratase activity would not have been expected from taking into account all of the prior art.

Applicants believe that all claims now presented are allowable over the cited prior art and a response to that effect is earnestly solicited.

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